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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/525,041	03/14/2000	Daniel R. Soppet	PF178D2	8342

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EXAMINER	
UNGAR, SUSAN NMN	
ART UNIT	**PAPER NUMBER**
1642	16

DATE MAILED: 08/13/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/525,041	Soppet et al
Examiner	**Art Unit**
Ungar	1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jul 3, 2002* .

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1, 9-17, and 21-124* is/are pending in the application.

4a) Of the above, claim(s) *1, 9-17, 38-45, 64-71, 90-97, and 116-123* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *21-37, 46-63, 72-89, 98-115, and 124* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

1. The Declaration (Paper No. 14) and the Response (Paper No. 13) filed July 3, 2002 in response to the Office Action of March 4, 2002 (Paper No. 12) are acknowledged and have been entered. Claims 21-37, 46-63, 72-89, 98-115 and 124 are currently being examined.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. The following rejections are maintained:

Claim Rejections - 35 USC § 112

4. Claims 21-37, 46-63, 72-89, 98-115 and 124 remain rejected under 35 USC 112, first paragraph for the reasons previously set forth in Paper No. 12, Section 4, pages 2-8.

Applicant argues that (a) the instant fact pattern is closely analogous to the situation presented in In Re Wands and cites the MPEP discussion of the case wherein since there was considerable direction and guidance in the specification, there was a high level of skill in the art at the time the application was filed and all of the methods needed to practice the invention were well known, that it would not require undue experimentation to practice the claimed invention, (b) methods of making antibodies were well known in the art at the time the invention was made and the specification describes various methods, (c) the specification describes how colon specific protein may be produced in a bacterial expression system, (d) the specification describes immunoassays and methods of making toxin linked antibodies, (e) the specification describes how to use antibodies to carry out *in vivo*

imaging so the instant specification teaches how to make and used the presently claimed antibodies and methods based thereon.

The argument has been considered but has not been found persuasive because (a)-(e) although the cited techniques are well known and the level of skill in the art was high at the time the invention was made the fact pattern in the instant application is not closely analogous to the situation presented in *In re Wands* because unlike the hepatitis B surface antigen of *In re Wands,* the Colon Specific Protein of the instant application is not well characterized or well known in the art and neither the specification nor the art of record teaches how to use the claimed invention because no function can be ascertained for the Colon Specific Protein and therefore no function can be ascertained for an antibody which binds said antigen. In particular, the specification teaches that the colon specific gene is found in all cells of the body. Thus, it appears that the although Applicant names the newly discovered gene as a colon specific gene, it is not colon specific. Further, the specification teaches that the expression product is primarily limited to the colon in non-diseased individuals and then teaches that the colon specific gene is overexpressed in colon cancer. The two teachings are confusing because they appear to be contradictory. However, even were colon specific RNA to be overexpressed in colon cancer, the claims are drawn to antibody which binds to protein, not to RNA and it cannot be determined from the information in the specification or in the art whether or not the protein encoded by the RNA is overexpressed in colon cancer compared to normal control for the reasons of record or that the expressed protein can be used for diagnosis or treatment of colon cancer

or any other type of cancer. Further, the claim are drawn to antibodies which bind to fragments or variants of SEQ ID NO:2 and it cannot be determined from the information in the specification or the art of record, what effects the impact of these variations would have on protein function, even if that function were known. Applicant's arguments have not been found persuasive and the rejection is maintained.

Applicant further argues that (f) the Bell Declaration demonstrates the production and characterization of polyclonal antibodies that bind to Colon Specific Protein wherein positive immunohistochemical staining for the Protein is seen in normal human colon and mRNA over-expression is seen in colon and intestinal cancers versus normal colon and intestinal tissues. Further, A review of the Declaration reveals that Dr. Bell states that since "the Colon Specific Gene appears to be overexpressed at the mRNA level in some human colon cancers.... the Colon Specific Protein is, therefore, also **likely** (emphasis added) to be overexpressed in some human colon cancers", (g) Applicant argues that for most genes the initiation of RNA is the most important point of control, hence when investigating the expression levels of a new gene and protein those of ordinary skill in the art most often look to mRNA expression levels as predictive of the relative protein levels.

The Declaration and the argument have been considered but have not been found persuasive because (f') there is no objective evidence demonstrating differential expression of the protein in colon cancer tissue compared to normal colon tissue. Although Dr. Bell states that it is likely that the protein is overexpressed in colon cancers compared to normal colon tissue, it is clear that Dr.

Bell is not able to predict that the Protein will be overexpressed in some human colon cancers since it is well known in the art that the expression of MRNA does neither dictate nor predict the translation of such mRNA into a polypeptide or an overexpressed polypeptide since the predictability of protein translation is not necessarily contingent on mRNA expression due to the multitude of homeostatic factors affecting transcription and translation, (g') the operative word here is "most". Contrary to Applicant's arguments, those of skill do not most often look to mRNA expression levels as predictive of the relative protein expression levels because it cannot be predicted, without empirical evidence, which mRNA expression levels are predictive of relative protein expression. This is especially true for uncharacterized molecules such as Colon Specific Protein. Applicant is invited to present objective evidence from the literature demonstrating that those of skill most often look to mRNA expression levels as predictive of the relative protein expression levels. Applicant's arguments have not been found persuasive and the rejection is maintained.

Applicant further argues that the protein is expressed *in vivo* as demonstrated by immunohistochemistry. The argument has been considered and has been found persuasive and this ground of rejection is withdrawn.

Applicant argues that the claims are drawn to antibodies which specifically bind to fragments of SEQ ID NO:2 and do not recite antibodies which bind to variants of SEQ ID NO:2. The argument has been considered but has not been found persuasive because the claims are drawn to antibodies produced by immunizing an animal with a protein selected from the group consisting of a

"protein which comprises an immunogenic fragment" of the amino acid sequence of SEQ ID NO:2, 30 amino acids of SEQ ID NO:2, 50 amino acids of SEQ ID NO:2. A protein that comprises an immunogenic fragment of SEQ ID NO:2, 30, 50 amino acids, reads on a protein that comprises 4-6, 50, 30 contiguous amino acids of SEQ ID NO:2 and also hundreds of other amino acids. The claim does not state that the immunogenic fragment, 30, 50 amino acids are exposed on the surface. The claim does not even require that the antibody bind to SEQ ID NO:2. The claims as currently written are drawn to a highly variant group of proteins which are variants of SEQ ID NO:2. Applicant's arguments have not been found persuasive and the rejection is maintained.

5. Claims 21-37, 46-63, 72-89, 98-115 and 124 remain rejected under 35 USC 112, first paragraph for the reasons previously set forth in Paper No. 12, Section 5, page 9.

Applicant argues that (a) the specification describes more than just antibodies which bind to the polypeptide of SEQ ID NO:2 and that the present invention encompasses antibodies which bind to immunogenic polypeptide fragments, 20 amino acid polypeptide fragments and 50 amino acid polypeptide fragments, (b) it is important to recognize that all the instant claims required that the antibody specifically binds to an amino acid sequence which is some portion of SE ID NO:2.

The argument has been considered but has not been found persuasive because (a') and (b) the claims are not limited to antibodies which bind to an amino acid sequence which is some portion of SEQ ID NO:2 for the reasons set forth above.

6. All other rejections and objections recited in Paper No.12 are withdrawn.

7. No claims allowed.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Ungar, PhD whose telephone number is (703) 305-2181. The examiner can normally be reached on Monday through Friday from 7:30am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached at (703) 308-3995. The fax phone number for this Art Unit is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Effective, February 7, 1998, the Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1642.

Susan Ungar
Primary Patent Examiner
August 9, 2002